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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/735,963 | 12/15/2003 | Jan Lindy Sorensen | 6567.200-US | 3391 |

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| EXAMINER |
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CHANG, CELIA C

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| ART UNIT | PAPER NUMBER |
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1625

DATE MAILED: 07/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/735,963

Applicant(s)

SORENSEN ET AL.

Examiner

Celia Chang

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above claim(s) 53-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-45 and 50-52 is/are rejected.
- 7) ☒ Claim(s) 46-49 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. Applicant's election of Group I, species of example 56 on page 65, claims 17-18 and claims 1-16, 19-52, 64 reading on the elected invention in the reply filed on April 28, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Based on the restriction and the species of election, the scope of $r=1$, piperidinyl compounds, Y is five membered monocyclic heteroaryl containing 3 heteroatoms is examined.

The requirement for further restriction among $r=0$ pyrrolidinyl core, $r=1$ piperidinyl core or $r=2$ azepidinyl core is hereby maintained for $r=1$ piperidinyl core based on the species election. The restriction among the different cores is proper because it is evidenced that the trihetero aromatic-pyrrolidinyl core is known to have protein kinase inhibition activity (CA 137:346240), the trihetero aromatic-piperidinyl core is known to have cholinergic activity (US 4,837,241) and the trihetero aromatic-azepidinyl core is known to have antipicornaviral activity (CA 115:159158), thus, the independent and distinct "cores" have been recognized by the art to be distinct class of compounds.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17-18 and the subject matter of claims 1-16, 19-52 wherein $r=1$, piperidinyl compounds, Y is five membered monocyclic heteroaryl containing 3 heteroatoms is examined. Claims 53-63 and the remaining subject of claims 1-16, 19-52 are withdrawn from consideration per 37 CFR 1.142(b). An advisory to rejoinder was made in the previous restriction action indicating rejoinable claims must be free from 112 issues. In a survey of the specification it was

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noted that none of the assay methods disclosed by the specification included any data or nexus to the claimed methods with any compounds. Thus, in view of the 112 issues in the process claims, none of the process claims will be rejoined with the elected product.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7-19, 23, 50 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Jensen et al. CA 109:6526 or Jensen et al. US 4,837,241.

See RN 129595-04-6, 114904-37-9, 114904-39-1, 114904-41-5, 114724-60-6, or 114904-44-8, which structural delineations from CAS have been provided. These compounds corresponding to pharmaceutical preparation of compounds disclosed in '241, col. 8, examples 6-8.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims s 1-5, 7-23, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al. US 4,837,241.

Determination of the scope and content of the prior art (MPEP §2141.01)

Jensen et al. '241 disclosed compounds for treating Alzheimer's disease as the claims and the anticipatory species were pointed out supra.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the broad scope of the claims wherein R4 is substituted alkyl, aryl or heteroaryl have not been exemplified. Generically, Jensen et al. '241 taught that the substituents on the Y moiety or the R1 moiety can optionally be substituted alkyl or aryl or heteroaryl (see col. 1-2 R' and R1 options).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the Jensen et al. '241 is in possession of the instant claims **because** one would expect all the compounds taught in Jensen et al. '241 to have similar activity. In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 7-22, 24-26, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosmans US 5,854,261.

Determination of the scope and content of the prior art (MPEP §2141.01)

Bosmans '261 disclosed therapeutic compounds having similar structure of the claims, see col. 1-2 formula I. The examples provided structurally close species to the instant claims, see table at col. 11-12.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the Bosmans examples is that instead of R1 being C1-6 alkoxy substituted alkyl, the species at col. 11-12, compound 5 or 6 have phenoxy moiety as R1. Generically, the "L" of the reference has been taught to be optionally alkoxy substituted alkyl or aryloxy substituted alkyl(see col. 2 lines 1-10).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art in possession of the Bosmans '261 is in possession of the instant claims **because** one would expect all the compounds taught in Bosmans '241 to have similar activity. The picking and choosing of optional alternative choices among Markush elements guided by the operable examples is prima facie obvious. In absence of unexpected results, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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Claims 1, 7-22, 24-28, 30-38, 42, are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohki et al. CA 129:54604 in view of Greene.

Determination of the scope and content of the prior art (MPEP §2141.01)

Ohki et al. disclosed hydroxyl protected intermediates i.e. reactant for making useful final products. The species has been structurally delineated as RN 208537-46-6.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the protected intermediate and the instant claims is that instead of ester protection, the instant claims have amide protection, i.e. A is NR^9R^{10} . Greene taught that for hydroxyl protection, one skilled in the art would expect the ester and amide protection to be optional choices for such compound (see pages 152-154, 158, 187, 189).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the chemical art in possession of the above references would be motivated to prepare the instantly claimed compounds wherein a is NR^9R^{10} **because** absent of unexpected results, there is nothing unobvious in picking the many hydroxyl protecting groups among the optional choices well recognized in the art by Greene.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-22, 24-41, 43-45, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gall et al. US 4,481,360 in view of King.

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Determination of the scope and content of the prior art (MPEP §2141.01)

Gall et al. '360 disclosed analgesic compounds having similar structure as the claims see formula at col. 26, col. 1-2 and compounds of claim 5 at col. 32.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between Gall et al. '360 compounds and the instant claims is that instead of R1 being pyridylalkyl i.e. R1 is alkyl optionally substituted with 4-pyridyl, the Gall et al. compounds have R1 being phenylalkyl. King taught that phenyl and pyridyl are bioisosteres (see table 1 ring equivalents).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art in possession of the above references would be motivated to modify the Gall '360 compounds with an bioisosteric replacement knowing that such replacement is expected to produce more compounds with similar activity i.e. an rational approach to finding new drugs (see whole article of King). The replacement of the operable prior art compounds of Gall '360 with an bioisosteric pyridyl is suggested by King with the well known recognition that such compounds would have structural analogue and similar activity (see p.207).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-22, 24-41, 43-45, 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gall et al. US 4,481,360 in view of Cuny et al. US 6,645,980.

Determination of the scope and content of the prior art (MPEP §2141.01)

Gall et al. disclosed structurally similar compounds having analgesic activity wherein the R1 moiety of the instant claims are phenylalkyl, see examples and dosage of the reference.

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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art is that instead of R1 being phenylalkyl, the instant claims are drawn to R1 being cycloalkylalkyl i.e. R1 is alkyl, substituted with cycloalkyl. Cury et al. '980 is analogous art which taught piperidinyl analgesic compound as Gall. Cury et al. '980 specifically demonstrated that in the replacement of the phenylethyl R1 moiety such as those disclosed by Gall examples, with a cyclohexylethyl (see col. 54, compound 6 vs. col. 124 compound 139) would not compromise the analgesic activity.

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

One having ordinary skill in the analgesic art in possession of the above references would be motivated to modify the Gall compounds with the replacement of the phenylethyl moiety with a cyclohexylethyl moiety **because** the art suggested that such modification would be successful in maintaining analgesic activity. It is prima facie obvious to one skilled in the art to employ attributes demonstrated in one operable compound i.g. Cury, in modification of another operable compound i.e. Gall since such attributes are known operable parameters in analogous art.


8. Claims 46-49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
July 6, 2006


Celia Chang
Primary Examiner
Art Unit 1625